Claims

1. A cobalamin derivative
(a) having no binding affinity or low binding affinity to transcobalamin II and
(b) retaining activity as a vitamin B12 substitute.

2. The cobalamin derivative according to claim 1
(a) having less than 20% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and
(b) retaining more than 2% of the activity as a vitamin B12 substitute in a growth assay.

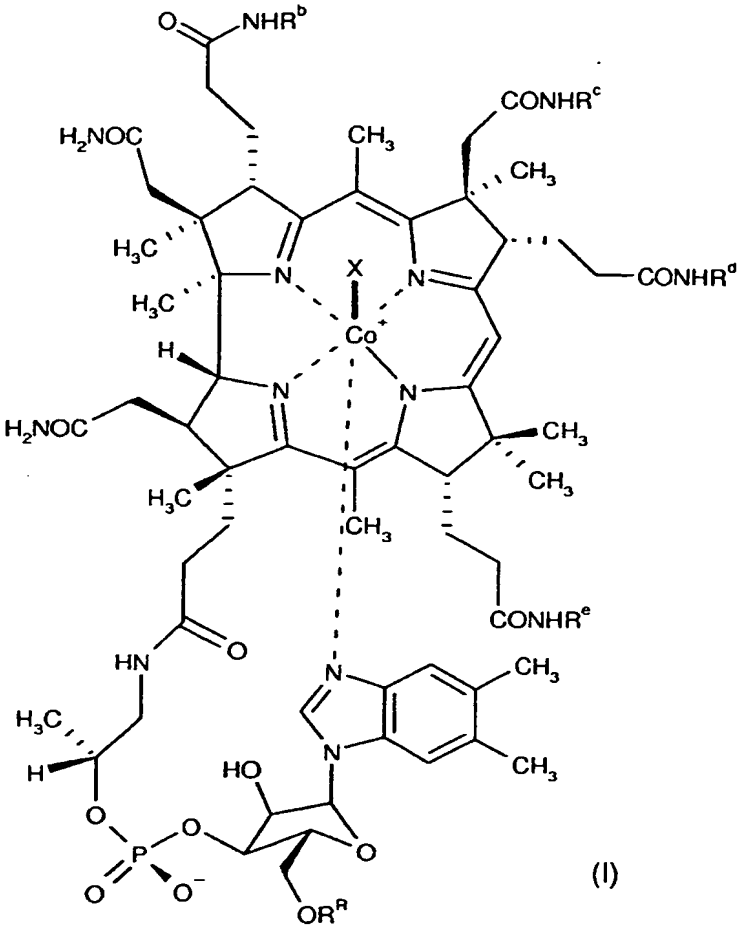
3. The cobalamin derivative according to claim 1
(a) having less than 10% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and
(b) retaining more than 10% of the activity as a vitamin B12 substitute in a growth assay.

4. The cobalamin derivative according to claim 1
(a) having less than 5% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and
(b) retaining more than 10% of the activity as a vitamin B12 substitute in a growth assay.

5. The cobalamin derivative according to anyone of claims 1 to 4 carrying a therapeutic and/or diagnostic agent.

6. The cobalamin derivative according to anyone of claims 1 to 5 carrying a radioactive metal.

7. The cobalamin derivative according to anyone of claims 1 to 6 of formula (I)



(I)

wherein

R^b, R^c, R^d and R^e, independently of each other, are a spacer-chelator group, an antibiotic or antiproliferative therapeutic agent, a sterically demanding organic group with 4 to 20 carbon atoms, or hydrogen;

R^R is a spacer-chelator group or an antibiotic or antiproliferative therapeutic agent, each connected through a linker Z, or hydrogen;

with the proviso that at least three of the residues R^b, R^c, R^d, R^e and R^R are hydrogen and at least one of the residues R^b, R^c, R^d and R^e is different from hydrogen;

X is a monodentate ligand; and

the central cobalt (Co) atom is optionally in the form of a radioactive isotope.

8. The cobalamin derivative according to claim 7 wherein R^e is hydrogen.

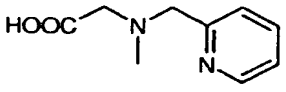
9. The cobalamin derivative according to claim 7 or 8 wherein the spacer-chelator group comprises

a spacer, which is an aliphatic chain of 2 to 10 carbon atoms, wherein one or two carbon atoms may be replaced by nitrogen and/or oxygen atoms and the aliphatic chain may be substituted by hydroxy, oxo or amino, and

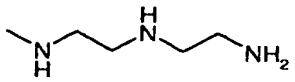
a chelator, which is a compound having two, three or more donor atoms selected from nitrogen, oxygen and sulfur in a distance such as to bind to a metal atom,

and optionally a metal atom.

10. The cobalamin derivative according to claim 9 wherein the chelator is selected from the chelators of formula (II) to (IX),



(II)



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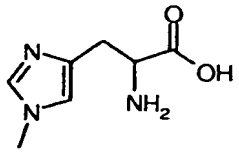

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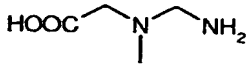

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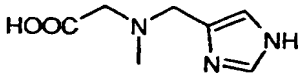

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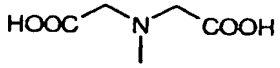

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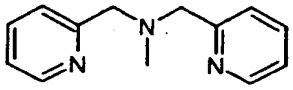
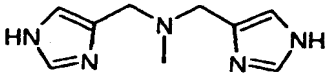


(VIII)



(IX)

wherein carboxyl groups may be present as esters.

11. The cobalamin derivative according to anyone of claims 6 to 10 wherein the radioactive metal is ^{94m}Tc, ^{99m}Tc, ^{188}Re, ^{186}Re, ^{111}In, ^{90}Y, ^{64}Cu, ^{67}Cu or ^{177}Lu.

12. The cobalamin derivative according to anyone of claims 7 to 11 wherein X is cyano, methyl, hydroxy, aquo or a 5'-deoxyadenosyl group

13. The cobalamin derivative according to claim 12 wherein X is cyano.

14. The cobalamin derivative according to anyone of claims 7 to 12 wherein the central cobalt atom is the radioisotope ^{57}Co or ^{60}Co.

15. The cobalamin derivative according to claim 10 wherein
R^b is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 2 to 4 carbon atoms, and the chelator is of formula (II), wherein the group COOH is optionally in the form of an ester;
R^c, R^d, R^e and R^R are hydrogen; and
X is cyano.

16. The cobalamin derivative according to claim 15 wherein
R^b is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 4 carbon atoms, and the chelator is of formula (II), wherein the group COOH is in the form of the ethyl ester;
R^c, R^d, R^e and R^R are hydrogen; and
X is cyano.

17. The cobalamin derivative according to claim 10 wherein
R^d is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 3 carbon atoms, and the chelator is of formula (II), wherein the group COOH is optionally in the form of an ester;
R^b, R^c, R^e and R^R are hydrogen; and
X is cyano.

18. The cobalamin derivative according to claim 10 wherein
R^b is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 2 carbon atoms, and the chelator is of formula (III);
R^c, R^d, R^e and R^R are hydrogen; and
X is cyano.

19. A pharmaceutical composition comprising a cobalamin derivative according to anyone of claims 1 to 18.

20. A method of diagnosis of a neoplastic disease or an infection by microorganisms in a mammal comprising
(a) exposing the mammal suspected of being inflicted by a neoplastic disease or an infection to a period of a vitamin B12 – free diet, and
(b) subsequently applying a cobalamin derivative according to anyone of claims 1 to 18 carrying a diagnostic agent.

21. A method of treatment of a mammal suffering from a neoplastic disease or an infection by microorganisms comprising
(a) exposing the mammal in need of treatment to a period of a vitamin B12 – free diet, and
(b) subsequently applying a cobalamin derivative according to anyone of claims 1 to 18 carrying a therapeutic agent.

22. Use of a cobalamin derivative according to anyone of claims 1 to 18 in a method of diagnosis of a neoplastic disease or an infection by microorganisms or in a method of treatment of a mammal suffering from a neoplastic disease or an infection by microorganisms.

23. The use according to claim 22 in cancer imaging.

24. Use of a cobalamin derivative according to anyone of claims 1 to 18 for the manufacture of a pharmaceutical composition for use in a method of diagnosis of a neoplastic disease or an infection by microorganisms or in a method of treatment of a mammal suffering from a neoplastic disease or an infection by microorganisms.

25. The use according to claim 24 of a cobalamin derivative for the manufacture of a pharmaceutical composition for cancer imaging.